EXHIBIT B

CLEAN VERSION OF ALL PENDING CLAIMS AS AMENDED HEREIN

(App'n No. To Be Assigned; Attorney Docket No. 9408-042-999)

Dated September 18, 2001

32. A method for detecting or measuring the presence of an alternatively spliced RNA transcript in a sample from a subject comprising the following steps in the order stated:

(a) contacting the nucleic acid sample in solution with one or more peptide-labeled oligonucleotide probes, comprising the sequence of a known splice-site junction, under conditions conducive to hybridization of the probes to nucleic acid in the sample; each probe comprising a first marker covalently attached to a first detectable label, and a second marker covalently attached to a second detectable label that produces a signal distinguishable from the first detectable label; such that one or more hybrid molecules are formed between the nucleic acid and one or more oligonucleotide probes;

(b) capturing at least one of the one or more hybrid molecules on a solid phase surface;

(c) contacting the solid phase surface with mung bean nuclease, under conditions wherein the nuclease is active;

(d) removing material not bound to the solid phase surface;

(e) detecting or measuring from the solid phase surface a first signal from the first detectable label and a second signal from the second detectable label;

(f) cleaving the hybrid molecules on the solid phase surface at mismatched base pairs; and

(g) detecting or measuring from the solid phase surface a third signal from the first detectable label and a fourth signal from the second detectable label, determining a first ratio of the second signal to the first signal, and a second ratio of the fourth signal to the third signal, and comparing the first ratio to the second ratio,

wherein a difference between the first ratio and the second ratio indicates that an alternatively spliced RNA transcript is in the sample.

33. A method for detecting or measuring the presence of an alternatively spliced RNA transcript in a sample from a subject comprising the following steps in the order stated:

(a) contacting the nucleic acid sample in solution with one or more peptide-labeled oligonucleotide probes, comprising the sequence of a known splice-site junction, under conditions conducive to hybridization of the probes to nucleic acid in the sample; each probe comprising a first and a second marker; such that one or more hybrid molecules are formed between the nucleic acid and one or more oligonucleotide probes;

(b) capturing at least one of the one or more hybrid molecules on a solid phase surface;

(c) contacting the solid phase surface with mung bean nuclease, under conditions wherein the nuclease is active;

(d) removing material not bound to the solid phase surface;

(e) contacting the solid phase surface with (i) a first partner molecule with the ability to specifically bind the first marker, and (ii) a second partner molecule with the ability to specifically bind the second marker, said first partner molecule comprising a first detectable label and said second partner molecule comprising a second detectable label that produces a signal distinguishable from the first detectable label;

(f) removing material not bound to the solid phase surface;

(g) detecting or measuring from the solid phase surface a first signal from the first detectable label and a second signal from the second detectable label;

(h) cleaving the hybrid molecules on the solid phase surface at mismatched base pairs; and

(i) detecting or measuring from the solid phase surface a third signal from the first detectable label and a fourth signal from the second detectable label, determining a first ratio of the second signal to the first signal, and a second

ratio of the fourth signal to the third signal, and comparing the first ratio to the second ratio,

wherein a difference between the first ratio and the second ratio indicates that an alternatively spliced RNA transcript is in the sample.

34. A method for detecting or measuring the presence of an alternatively spliced RNA transcript in a sample from a subject comprising:

(a) contacting the nucleic acid sample in solution with one or more peptide-labeled oligonucleotide probes comprising the sequence of a known splice-site junction sequence, under conditions conducive to hybridization of the probes to nucleic acid in the sample; each probe comprising a first and a second marker; such that one or more hybrid molecules are formed between the nucleic acid and one or more oligonucleotide probes;

(b) capturing at least one of the one or more hybrid molecules on a solid phase surface;

(c) contacting the solid phase surface with mung bean nuclease, under conditions wherein the nuclease is active;

(d) removing material not bound to the solid phase surface;

(e) contacting the solid phase surface with a first primary partner molecule, with the ability to bind the first marker, and a second primary partner molecule with the ability to bind the second marker;

(f) removing material not bound to the solid phase surface;

(g) contacting the solid phase surface with a first secondary partner molecule, with the ability to bind the first primary partner molecule, said first secondary partner molecule comprising a first detectable label, and a second secondary partner molecule, with the ability to bind the second primary partner molecule, said second secondary partner molecule comprising a second detectable label that produces a signal distinguishable from the first detectable label;

(h) removing material not bound to the solid phase surface;

(i) detecting or measuring a first signal from the first detectable label and a second signal from the second detectable label;

(j) cleaving the hybrid molecules at mismatched base pairs; and

(k) detecting or measuring a third signal from the first detectable label and a fourth signal from the second detectable label, determining a first ratio of the second signal to the first signal, and a second ratio of the fourth signal to the third signal, and comparing the first ratio to the second ratio,

wherein a difference between the first ratio and the second ratio indicates that an alternatively spliced RNA transcript is in the sample.

35. A method for detecting or measuring the presence of an alternatively spliced RNA transcript in a sample from a subject comprising the following steps in the order stated:

(a) contacting the nucleic acid sample in solution with one or more peptide-labeled oligonucleotide probes comprising the sequence of a known splice-site junction sequence, under conditions conducive to hybridization of the probes to nucleic acid in the sample; each probe comprising a first marker covalently attached to a first detectable label, and a second marker covalently attached to a second detectable label that produces a signal distinguishable from the first detectable label; such that one or more hybrid molecules are formed between the nucleic acid and one or more oligonucleotide probes;

(b) capturing at least one of the one or more hybrid molecules on a solid phase surface;

(c) contacting the solid phase surface with mung bean nuclease, under conditions wherein the nuclease is active;

(d) removing material not bound to the solid phase surface;

(e) detecting or measuring a first signal from the first detectable label and a second signal from the second detectable label;

(f) cleaving the hybrid molecules at mismatched base pairs; and

(g) detecting or measuring a third signal from the first detectable label and a fourth signal from the second detectable label, determining a first ratio of the second signal to the first signal, and a second ratio of the fourth signal to the third signal, and comparing the first ratio to the second ratio,

wherein the first ratio at least 35% greater than the second ratio indicates that an alternatively spliced RNA transcript is in the sample.

36. A method for detecting or measuring the presence of an alternatively spliced RNA transcript in a sample from a subject comprising the following steps in the order stated:

(a) contacting the nucleic acid sample in solution with one or more peptide-labeled oligonucleotide probes comprising the sequence of a known splice-site junction sequence, under conditions conducive to hybridization of the probes to nucleic acid in the sample; each probe comprising a first and a second marker; such that one or more hybrid molecules are formed between the nucleic acid and one or more oligonucleotide probes;

(b) capturing at least one of the one or more hybrid molecules on a solid phase surface;

(c) contacting the solid phase surface with mung bean nuclease, under conditions wherein the nuclease is active;

(d) removing material not bound to the solid phase surface;

(e) contacting the first marker with a first partner molecule and the second marker with a second partner molecule, said first partner molecule comprising a first detectable label and said second partner molecule comprising a second detectable label that produces a signal distinguishable from the first detectable label;

(f) removing material not bound to the solid phase surface;

(g) detecting or measuring a first signal from the first detectable label and a second signal from the second detectable label;

(h) cleaving the hybrid molecules at mismatched base pairs; and

(i) detecting or measuring a third signal from the first detectable label and a fourth signal from the second detectable label, determining a first ratio of the second signal to the first signal, and a second ratio of the fourth signal to the third signal, and comparing the first ratio to the second ratio,

wherein the first ratio at least 35% greater than the second ratio indicates that an alternatively spliced RNA is in the sample.

37. A method for detecting or measuring the presence of an alternatively spliced RNA transcript in a sample from a subject comprising:

(a) contacting the nucleic acid sample in solution with one or more peptide-labeled oligonucleotide probes comprising the sequence of a known splice-site junction sequence, under conditions conducive to hybridization of the probes to nucleic acid in the sample; each probe comprising a first and a second marker; such that one or more hybrid molecules are formed between the nucleic acid and one or more oligonucleotide probes;

(b) capturing at least one of the one or more hybrid molecules on a solid phase surface;

(c) contacting the solid phase surface with mung bean nuclease, under conditions wherein the nuclease is active;

(d) removing material not bound to the solid phase surface;

(e) contacting the solid phase surface with a first primary partner molecule, with the ability to bind the first marker, and a second primary partner molecule with the ability to bind the second marker;

(f) removing material not bound to the solid phase surface;

(g) contacting the solid phase surface with (i) a first secondary partner molecule, with the ability to bind the first primary partner molecule, said first secondary partner molecule comprising a first detectable label, and (ii) a second secondary partner molecule, with the ability to bind the second primary partner molecule, said second secondary partner molecule comprising a second detectable label that produces a signal distinguishable from the first detectable label;

(h) removing material not bound to the solid phase surface;

(i) detecting or measuring from the solid phase surface a first signal from the first detectable label and a second signal from the second detectable label;

(j) cleaving the hybrid molecules on the solid phase surface at mismatched base pairs; and

(k) detecting or measuring from the solid phase surface a third signal from the first detectable label and a fourth signal from the second detectable label, determining a first ratio of the second signal to the first signal, and a second ratio of the fourth signal to the third signal, and comparing the first ratio to the second ratio,

wherein the first ratio at least 35% greater than the second ratio indicates that an alternatively spliced RNA transcript is in the sample.

44. A two-molecule peptide-labeled oligonucleotide probe comprising a first molecule comprising a first sequence of nucleotides, which molecule is covalently attached to a peptide label; and a second molecule comprising a second sequence of nucleotides complementary to the first sequence and contiguous with additional nucleotides complementary to a wild-type or variant form of a nucleotide polymorphism of interest and its flanking regions.

45. A two-molecule peptide-labeled oligonucleotide probe comprising a first molecule, the nucleotide sequence of which consists of a first sequence of from 15 to 25 nucleotides, which molecule is covalently attached to a peptide label; and a second molecule, the nucleotide sequence of which consists of a second sequence of from 15 to 25 nucleotides complementary to the first sequence and contiguous with from 30 to 40 nucleotides complementary to a wild-type or variant form of a nucleotide polymorphism of interest and its flanking regions.

46. The probe of claim 44 or 45, wherein the second molecule comprises at least one detectable marker.

47. The probe of claim 46, wherein at least one detectable marker is a fluorophore.

48. The probe of claim 44 or 45, wherein at least one nuclease-resistant nucleotide base derivative occurs at a position within three nucleotides from the transition from double-stranded to single-stranded structure when the first molecule is hybridized to the second molecule.

49. The probe of claim 44 or 45, wherein six nuclease-resistant nucleotide base derivatives occur at positions within three nucleotides from the transition from double-stranded to single-stranded structure when the first molecule is hybridized to the second molecule.

50. A kit comprising in one or more containers a purified first molecule comprising a first sequence of nucleotides, which molecule is covalently attached to a peptide label, and a purified second molecule comprising a second sequence of nucleotides complementary to the first sequence and contiguous with additional nucleotides complementary to a wild-type or variant form of a nucleotide polymorphism of interest and its flanking regions.